REMARKS

I. Status of the Claims

With entry of this amendment, claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33-37, and 39 are pending in this application. Claims 34-37 are withdrawn from further consideration under 37 C.F.R. § 1.142(b).

Claims 1-7, 20-27, 30-33, 38 and 39 stand rejected under 35 U.S.C. § 102. Claims 1-33, 38 and 39 are rejected under 35 U.S.C. § 112. Applicants cancel claims 1-3, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 38 without disclaimer of or prejudice to the subject matter recited therein, rendering the rejection of these claims moot.

II. Status of Prior Objections and Rejections

A. The objection to the abstract is withdrawn. Office Action, at page 2.

B. The objection to the Declaration and Power of Attorney is withdrawn. *Id.*, at pages 2-3.

C. The rejection of claim 4 under 35 U.S.C. § 102(a) as allegedly being anticipated by Aihara *et al.* is withdrawn. *Id.*, at pages 3-4.

D. The rejection of claims 1-7, 20-25, 28, 29, and 30-33 under 35 U.S.C. § 102(e) as allegedly being anticipated by Chien *et al.* is withdrawn. *Id.*, at pages 8-9.

E. The rejection of claims 1-5, 8, 9, and 12-15 under 35 U.S.C. § 102(b) as allegedly being anticipated by Philip *et al.* is withdrawn. *Id.*, at page 9.

F. The rejection of claims 1-5, and 10-12 under 35 U.S.C. § 102(b) as allegedly being anticipated by Alarco *et al.* is withdrawn. *Id.*, at pages 9-10.

G. The rejection of claims 1-5, 16, and 17 under 35 U.S.C. § 102(b) as allegedly being anticipated by Mohuczy *et al.* is withdrawn. *Id.*, at page 10.

H. The rejection of claims 1-5, 18, and 19 under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen *et al.* is withdrawn. *Id.*, at page 11.

III. The Claims Are Not Anticipated

A. The Examiner maintains the rejection of claims 1 and 2 under 35 U.S.C. § 102(a) as allegedly being anticipated by Aihara *et al.* (GenBank Accession Number AF131884, Database DDBJ, submitted February 15, 2000). Office Action, at pages 3-6.

Solely to advance prosecution, and without acquiescing in the rejection, Applicants cancel claims 1 and 2 without disclaimer of or prejudice to the subject matter recited therein. Therefore, Applicants respectfully submit that the Examiner's rejection of claims 1 and 2 is moot.

B. The Examiner also maintains the rejection of claims 1-7, 20-27, 30-33, 38, and 39 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kuo *et al.* (Development, 126:4223-4234, 1999). *Id.*, at pages 6-8. The Examiner alleges that "[t]he disclosure of Kuo *et al.* meets all the structural limitations of the claims, and therefore is considered to

possess the functional limitations of the claim, namely to [sic] ability to induce cardiac-specific expression *in vivo* of genes operably linked to the polypeptide." *Id.* at page 8.[1]

Applicants respectfully traverse for the reasons of record, and for the following additional reasons. In *Regents of the University of California v. Eli Lilly & Co.*, the Federal Circuit held that the sequence of rat insulin does not provide an adequate written description of the cDNA encoding human insulin. 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). According to the Court, "an adequate written description of a DNA requires . . . a description of the DNA itself." *Id.* at 1404 (citation omitted).

Claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 recite sequences from the human CARP gene. Kuo *et al.* do not disclose the nucleotide sequence of the polynucleotide upstream of the gene encoding human CARP (i.e., SEQ ID NO:2). Instead, Kuo *et al.* disclose only the mouse CARP gene and the activity of 5' *cis* regulatory elements. Based on the *Lilly* decision, Kuo *et al.* fail to provide adequate written description and do not anticipate claims to human CARP gene polynucleotides. Accordingly, Applicants respectfully assert that claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 are not anticipated by Kuo *et al.*

[1] The Examiner also contends that Kuo *et al.* anticipate the claims because one skilled in the art would reasonably conclude that a polynucleotide comprising a >20 bp fragment of SEQ ID NO:1 or SEQ ID NO:2 would be able to induce cardiac-specific expression *in vivo* of genes operably linked to the polynucleotide. *Id.*, at pages 7-8. Applicants submit that the Examiner has provided no evidence that one skilled in the art would have a basis for concluding that a polynucleotide comprising a >20 bp fragment of SEQ ID NO:1 or SEQ ID NO:2 would be able to induce cardiac-specific expression *in vivo* of genes operably linked to the polynucleotide.

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 4, 5, 7, 21, 23, 25, 27, 31, 33, and 39 under 35 U.S.C. § 102(b) as anticipated by Kuo *et al.* The rejection of claims 1-3, 6, 20, 22, 24, 26, 30, 32, and 38 is moot.

IV. The Specification Enables the Claims

The Examiner rejects claims 1-33, 38 and 39 under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. Office Action, at page 11. The Examiner asserts that "[i]t is unclear whether the Specification present [sic] any examples wherein the CARP promoter without the cooperation of inverted terminal repeat (ITR) sequences from human adeno-associated virus (AAV) are [sic] effective in achieving cardiac tissue-specific transcription of transgenes *in vivo*. *Id.*, at page 14. In support of her assertion, the Examiner refers to Example 7 and Figure 6A of the specification, and contends that "it is unclear whether the specification (including Example 10) clearly teaches that the instant invention, does not require inverted terminal repeat sequences . . . since pXL3759, in Figure 6, clearly contains inverted terminal repeat sequence (ITRs)." *Id.*, at page 13.

In addition, the Examiner alleges that Chien *et al.*(WO 00/15821) teach that the CARP promoter without AAV-ITR does not exhibit transgene expression, and that Fu *et al.* (Nature Biotechnology, 16:253-257, 1998) show that the inclusion of both the left and right end segments of the AAV-ITR sequences impart the ability to enhance the level as well as tissue specificity of the transgene expression using viral gene promoters or

tissue-specific cellular gene promoters. *Id.*, at pages 13-14. The Examiner concludes that "using the polynucleotide sequence upstream of the CARP gene as a promoter to induce expression of a transgene in cardiac cells *in vivo* is unpredictable," and alleges that "to practice the invention claimed one skilled in the art would need to undergo undue trial and error experimentation, beyond the teachings of the instant specification." *Id.*, at pages 14-15.

Applicants respectfully traverse. Example 10 clearly demonstrates cardiac-specific expression of a transgene following administration of plasmid pXL3634 (*see* Specification, at paragraphs 83 and 134-140, and Figure 8). In contrast to the plasmids disclosed by Fu *et al.*, plasmid pXL3634 does not contain inverted terminal repeat (ITR) sequences from human adeno-associated virus (AAV). In fact, Example 7 clearly discloses, the "expression cassette [is] identical to that of the plasmid pXL3634" (*see* Specification, at paragraph 119), which is devoid of ITR sequences (*see* Figure 3). Therefore, in contrast to the Examiner's assertion, Applicants have provided specific guidance by which one skilled in the art could induce gene expression in cardiac cells *in vivo* using a polynucleotide comprising a fragment of the CARP promoter in the absence of inverted terminal repeat (ITR) sequences from human adeno-associated virus (AAV).

Applicants further submit that plasmid pXL3759 is not used to achieve the CARP promoter-induced transgene expression *in vivo*. Instead, pXL3759 is used to construct the adenovirus depicted in Figure 6B. Accordingly, the ITR sequences from pXL3759 are used to control adenoviral DNA replication. The ITR sequences are outside the

expression cassette and are not necessary for the CARP promoter to mediate cardiac-specific transgene expression *in vivo*.

Applicants respectfully submit that the Examiner has improperly applied Chien *et al.* as evidence of nonenablement. As discussed above, Example 10 and Figure 8 disclose transgene expression following intracardiac administration of a plasmid vector, which is devoid of AAV-ITR sequences. In contrast, Chien *et al.* only disclose cardiac expression of a reporter gene following adenovirus infection (*see* Example 1 and Figure 2).

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. The rejection of claims 1-3, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 38 is moot.

V. Conclusion

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 in condition for allowance.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented some new arguments as to the application of the art against Applicants' invention. It is respectfully submitted that the entering of the Amendment

would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the Amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants respectfully submit that the claimed invention, as amended, is not anticipated by the prior art references cited by the Examiner. In addition, Applicants submit that the specification enables the full scope of the claims. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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